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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,970	02/24/2004	Joan H. M. Knoll	30307-CNT1	5467

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ERICKSON & KLEYPAS, L.L.C.
800 W. 47TH STREET, SUITE 401
KANSAS CITY, MO 64112

EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/786,970	KNOLL ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *1-8,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II, claims 9 and 10, in the reply filed on February 26, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 9 and 10 are drawn to the elected invention and have been examined herein. Claims 1-8, 11 and 12 are withdrawn from consideration as being drawn to a non-elected invention.

Sequence Listing

3. On August 16, 2004, Applicant filed a paper copy of the sequence listing and requested that the CRF copy of the sequence listing filed in U.S. Application 09/573,080 be transferred to the present application. The letter filed August 16, 2004, notes a requirement to state that the "the Computer Readable Sequence listing submitted with this application is identical to "the Computer Readable Form submitted with application Serial No. 09/573,080." However, this letter was not accompanied by the required statement that the CRF copy of the sequence listing filed in 09/573,080 is identical to the paper copy of the sequence listing filed in the present application on August 16, 2004. Further, the originally filed application was filed with a compact disk including the text of the sequence listing and the first page of the specification indicates that the CRF copy of the sequence listing filed in 09/573,080 is identical to sequence listing filed on February 24, 2004. However, this statement referred to the sequence listing filed on the

CD-Rom, and not the paper copy of the sequence listing subsequently filed on August 16, 2004. It is noted that the sequence listing on a CD-ROM on February 24, 2004 is not in compliance because a duplicate copy of the CD was not provided, and the discs contained files that are non-ASCII files. Further, it is noted that when portions of an application are contained on a compact disc, the paper portion of the specification must identify the compact disc(s) and list the files including name, file size, and creation date on each of the compact discs. See 37 CFR 1.52(e).

Drawings

4. Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See, for example, page 11. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112 – Written Description

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In analyzing claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note that with regard to genus/species situations, a "Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial

structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof.

Thereby, to ascertain whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. It is then determined whether a representative number of species have been defined by other identifying characteristics. In the present situation, claim 9 is drawn to a method for developing a hybridization probe comprising determining a sequence of a single copy sequence by ascertaining the nucleotide by nucleotide sequence of a target nucleic acid sequence, comparing the target nucleic acid sequence with known repeat sequences, identifying said single copy sequence from the comparison, and developing a hybridization probe from the non-repetitive portion of the target nucleic acid, wherein the repeat sequences appear at least 10 times in the genome and are at least about 50 nucleotides in length. Claim 10 is drawn to a method for identifying a single copy sequence interval in a target nucleic acid comprising ascertaining the nucleotide by nucleotide sequence of a target nucleic acid sequence, comparing the target nucleic acid sequence with known repeat sequences using a computer program and identifying said single copy sequence from the comparison wherein the repeat sequences appear at least 10 times in the genome and are at least about 50 nucleotides in length.

The specification discloses repeat sequences identified in the human genome and consisting of the sequences of SEQ ID NO: 1-428 and 447-479. Accordingly, the specification teaches the complete structure of the repeat sequences consisting of SEQ

ID NO: 1-428 and 447-479. However, the present claims require the use of "known" repeat sequences, wherein the repeat sequences are defined only in terms of the fact that they occur at least 10 times in a genome and are at least 50 nucleotides in length. The claims do not define the "known" repeat sequences in terms of any other structural features, such as their nucleotide sequence, the sequence identity they share with other sequences, etc. Further, what constitutes a known sequence varies over time and with one's interpretation of this term. While a repeat sequence may be known to one researcher, that same repeat sequence may not be known to the general public. Similarly a repeat sequence may be "known" in that it exists in an organism, but the actual nucleotide sequence and identity of the repeat sequence may not have been characterized. The human genome and the genome of other organisms, including all animals, plants, and microorganisms are expected to include a substantially large number of repeat sequences, differing from one in another in terms of their nucleotide sequence, length and frequency. Thereby, the disclosure of the specific sequences of SEQ ID NO: 1-428 and 447-479 is not considered to constitute a representative number of the claimed "known repeat sequences" which are not defined in terms of any relevant structural limitations.

It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. restriction map, biological activity of an encoded protein product, etc.). In the present application, no additional members of the claimed genus have been described by other relevant identifying characteristics other than the length of the repeat sequence being greater

than 50 nucleotides. However, this recitation does not serve to meaningfully distinguish the claimed repeat sequences over other sequences. Further, no repeat sequences have been provided that were obtained from non-human organisms, such as vertebrates, plants or microorganisms.

Additionally, the specification does not disclose a clear relationship between the structure and function of the claimed "known repeat sequences."

In the absence of a representative number of species of the claimed genus, there is insufficient descriptive support for the currently claimed genus of any "known repeat sequences" obtained from any human or any non-human organism.

The decisional law in this area has been very consistent. The Federal Circuit in Lilly, Fiers, Rochester and many other cases has determined that the written description issue applies to situations where the definition of the subject matter of the claims fails to provide description commensurate with the genus. The most recent case law directly supports this rejection. As the District Court in University of Rochester v. G.D. Searle & Co., Inc. (2003 WL 759719 W.D.N.Y.,2003. March 5, 2003.) noted "In effect, then, the '850 patent claims a method that cannot be practiced until one discovers a compound that was not in the possession of, or known to, the inventors themselves. Putting the claimed method into practice awaited someone actually discovering a necessary component of the invention." This is similar to the current situation since the breadth of the current claims comprises the use of repeat sequences which the present inventors were not in the possession of, or which were not known to the inventors. In a genus

that is possibly quite immense, the specification discloses only a limited number of embodiments – that is the sequences of SEQ ID NO: 1-428 and 447-479.

As noted in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), the Federal Circuit concluded that:

"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

This finding is also emphasized in *Ex Parte Kubin* (No. 2007-0819, Bd. Pat. App. & Int. May 31, 2007), wherein it is stated that :

"Although there is often significant overlap" between the enablement and written description requirements, "they are nonetheless independent of each other." University of Rochester, 358 F.3d at 921, 69 USPQ2d at 1891. An "invention may be enabled even though it has not been described." Id. Such is the situation here. While we conclude one skilled in the art would have been able to make and use the full scope of claim 73 through routine experimentation, we find Appellants did not describe the invention of claim 73 sufficiently to show they had possession of the claimed genus of nucleic acids. See, e.g., Noelle v. Lederman, 355 F.3d 1343, 1348, 69 USPQ2d 1508, 1513 (Fed. Cir. 2004) ("invention is, for purposes of the 'written description' inquiry, whatever is now claimed").

Further, "Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural

features. *See University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895." Thereby, a showing of how to potentially identify and make other repeat sequences is not sufficient to establish that Applicant's were in possession of the invention as broadly claimed.

Accordingly, there is no record or description which would demonstrate conception of any repeat sequences from any human or non-human organism other than those expressly disclosed as the human repeat sequences of SEQ ID NO: 1-428 and 447-479. Therefore, the claims fail to meet the written description requirement because the claims encompass a significantly large genus of polynucleotide sequences which are not described in the specification.

Claim Rejections - 35 USC § 112 second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 10 are indefinite over the recitation of "known repeat sequence". What constitutes a known repeat sequence varies over time, such that what repeat sequence is unknown today, may become known tomorrow. In addition, a sequence that is "unknown" to one individual (e.g., because it is not in a public database), may be known to another individual who is performing research on this sequence. Also, a

repeat sequence may be known because it exists in nature, but the specific nucleotide structure or the location in a genome of the sequence may not have been characterized. Since what constitutes "known" changes over time, and may vary depending on the individual and the interpretation of what is known, there is not a fixed and complete definition for what constitutes the "known repeat sequence." Accordingly, one of skill in the art cannot determine the meets and bounds of the claimed subject matter.

Claims 9 and 10 are indefinite over the recitation of "determining the sequence of at least one single copy sequence in said target nucleic acid computationally" (claim 9) and "identifying a single copy sequence interval from a target nucleic acid sequence computationally" (claim 10) because it is unclear as to how the recitation of "computationally" is intended to further limit the claims since the determining and identifying steps as further defined in the claims do not include the use of a computer or other numerical means.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 9 and 10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No.6,828,097. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of '097 are both inclusive of methods of developing hybridization probes and identifying a single copy sequence interval comprising determining the sequence of a single copy sequence in a target nucleic acid by ascertaining the nucleotide-by-nucleotide sequence of the target nucleic acid, comparing the ascertained sequence to known repeat sequences, identifying a single copy sequence from the comparison and developing a hybridization probe to a portion of the single-copy sequence. While the claims of '097 are limited to particular known repeat sequences, the present claims encompass any repeat sequence and thereby encompass the repeat sequences recited in '097.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 9 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Kazazian et al (U.S. Patent NO. 6150160).

Kazazian (col. 42) teaches methods of identifying a single copy sequence interval and methods of developing a hybridization probe to a single copy sequence interval comprising determining the nucleotide-by-nucleotide sequence of a target nucleic acid, comparing the ascertained nucleotide sequence to repeat sequences present in databases using BLAST (i.e., a computer program), identifying single copy sequences that do not include repetitive sequences, and developing hybridization probes comprising sequences that are complementary to the non-repetitive portion of the target nucleic acid and comprising at least a portion of the single copy sequence.

Specifically, Kazazian (col. 27, lines 24-34) teaches:

"The empty sites for insertions A-D were amplified by PCR using oligonucleotide primers that flanked the insertion site. The sequence flanking each empty site was checked for repetitive sequences using the BLAST algorithm (BCM search launcher) to scan the sequences in GenBank and an EST database (Altschul, et al., 1990, J Mol. Biol. 215:403-410). Sequences in non-repetitive DNA flanking each insertion were used to design oligonucleotide probes. Those probes were used in PCR reactions with HeLa cell genomic DNA. In every case, a single band of the predicted size was amplified."

Kazazian (col. 42) further teaches:

"Southern blot analysis was carried out on the DNAS of 19-25 different individuals using probes flanking each of the newly isolated active L1s. The 5' flank of each L1 was checked for repetitive sequences by use of the BLAST (Altschul et al.

1990. *J Mol Biol.* 215: 403-410) algorithm (BCM search launcher).Single copy probes were generated by PCR and ranged from 300-00 bp."

In the method of Kazazian, the nucleotide sequences are compared to all repeat sequences present in the GenBank and EST database, which necessarily includes repeat sequences that occur within a genome at least 10 times and which are of a length of at least 50 nucleotides. For example, Kazazian teaches screening the newly identified flanking sequences containing single-copy nucleic acids for the presence of L1 sequences, which are present 30-60 times in the average diploid human genome and are of a length of greater than 50 nucleotides (col. 1, line 49-col. 2, line 10; col. 39, lines 27-40; col. 47, lines 25-42).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Carla Myers/
Primary Examiner, Art Unit 1634